Claims

1. Use of a compound comprising a structure of the general formula (I)

$$-N' - X - Y - N'' - \qquad (I)$$

wherein X represents one atom and Y represents at least one atom and X and Y may individually be substituted at least once, and

N' and N'' are nitrogen,

or comprising a compound being a moiety of gentamicin,

or a pharmaceutically acceptable addition salt or hydrate thereof,

for the manufacture of a medicament for the prophylaxis and/or treatment of induced cell toxicity.

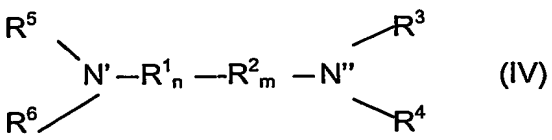
2. The use according to claim 1, wherein the compound comprises a structure of the general formula (II)

$$-N' - C - C - N'' - \qquad (II)$$

3. The use according to claim 1, wherein the compound comprises a structure of the general formula (III)

$$-N' - C - N - C - N'' - \qquad (III)$$

4. Use of a compound comprising a structure of the general formula (IV)



(IV)

wherein

each R^1 and each R^2 independently are selected from C, S, N, O, optionally substituted with C, S, N, O, OH, hydrogen, alkyl, alkenyl, alkynyl, phenyl, benzyl, amine (NH), halogen, substituted lower alkyl, aryl, heterocycloalkyl, heteroaryl, aryl-(C_{1-4})-alkyl, heteroaryl-(C_{1-4})-alkyl, heterocyclyl-(C_{1-4})-alkyl, cycloalkylalkyl, cycloalkyl, optionally further substituted one or more times with C, S, N, O, OH, phenyl, amine (NH), halogen, substituted lower alkyl, aryl, heterocyclyl, heteroaryl, aryl-(C_{1-4})-alkyl, heteroaryl-(C_{1-4})-alkyl, heterocyclyl-(C_{1-4})-alkyl, cycloalkylalkyl, cycloalkyl, alkoxy, carboxy, halogen, trifluoromethyl, cyano, amino, or nitro, and wherein

$_m$ is an integer of from 1 to 8,

$_n$ is an integer of from 1 to 8,

N' and N" are nitrogen,

R^3, R^4, R^5 and R^6 are independently selected from C, S, N, O, OH, hydrogen, alkyl, alkenyl, alkynyl, phenyl, benzyl, amine (NH), halogen, substituted lower alkyl, aryl, heterocycloalkyl, heteroaryl, aryl-(C_{1-4})-alkyl, heteroaryl-(C_{1-4})-alkyl, heterocyclyl-(C_{1-4})-alkyl, cycloalkylalkyl, cycloalkyl, optionally further substituted one or more times with C, S, N, O, OH, phenyl, amine (NH), halogen, substituted lower alkyl, aryl, heterocyclyl, heteroaryl, aryl-(C_{1-4})-alkyl, heteroaryl-(C_{1-4})-alkyl, heterocyclyl-(C_{1-4})-alkyl, cycloalkylalkyl, cycloalkyl, alkoxy, carboxy, halogen, trifluoromethyl, cyano, amino, or nitro,

or one or more of R^3, R^4, R^5 and R^6 is a chemical bond,

or a pharmaceutically acceptable addition salt or hydrate thereof,

for the manufacture of a medicament for the prophylaxis and/or treatment of induced cell toxicity.

5. The use according to claim 4, wherein at least one of R^3, R^4, R^5 and R^6 is H.

6. The use according to claim 4, wherein R^3 and R^5 are H.

7. The use according to any of the preceding claims, wherein R^6 and R^2 form a ring.

8. The use according to the claims 4-7, wherein R^4 and R^1 form a ring.

9. The use according to the claims 4-7, wherein R^4 and R^6 form a ring.

10. The use according to the claims 4-7, wherein R^4 and N' form a ring.

11. The use according to the claims 4-7, wherein R^6 and N" form a ring.

12. The use according to the claims 8-11, wherein the ring is 5-membered.

13. The use according to the claims 8-11, wherein the ring is 6-membered.

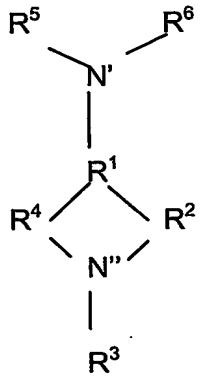
14. The use according to the claims 8-11, wherein the ring is 7-membered.

15. The use according to claim 4, wherein at least three of R^3 to R^6 are a chemical bond.

16. The use according to claim 4, wherein at least two of R^3 to R^6 are a chemical bond.

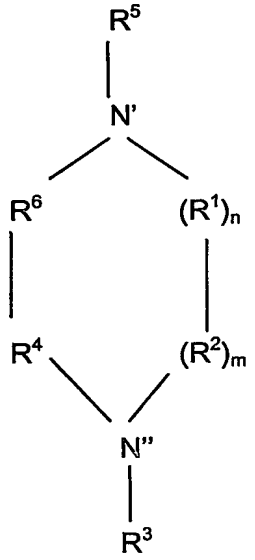
17. The use according to claim 4, wherein at least one of R^3 to R^5 is a chemical bond.

18. The use according to any one the preceding claims, wherein the compound has a structure of the general formula (V)



(V)

or the general formula (VI)



(VI)

wherein

N' and N", $_m$, $_n$, R^1, R^2, R^3, R^4, R^5 and R^6 are as defined in the claims 1-17, or a pharmaceutically acceptable addition salt or hydrate thereof, for the manufacture of a medicament for the prophylaxis and/or treatment of induced cell toxicity.

19. The use according to any of the preceding claims, wherein said cell presents the receptor megalin and/or the receptor cubilin.

20. The use according to any of the preceding claims, wherein at least one of R^1 or R^2 is C.

21. The use according to any of the claims 1-19, wherein R^1 and R^2 are C.

22. The use according to any of the claims 1-19, wherein at least one of R^1 or R^2 is S.

23. The use according to any of the claims 1-19, wherein R^1 and R^2 are S.

24. The use according to any of the claims 1-19, wherein at least one of R^1 and R^2 is N.

25. The use according to any of the claims 1-19, wherein R^1 and R^2 are N.

26. The use according to any of the claims 1-19, wherein at least one of R^1 and R^2 is O.

27. The use according to any of the claims 1-19, wherein R^1 and R^2 are O.

28. The use according to any of the preceding claims, wherein the medicament is capable of binding to the receptor megalin and/or the receptor cubilin.

29. The use according to claim 1, wherein the compound is selected from diaminomethane, 1,2-diaminoethane, 1,3-diaminopropane, 1,4-diaminobutane, 1,5-diaminopentane, 1,6-diaminohexane, 1,7-diaminoheptane, 1,8-diaminooctane, 3-methylamino-1-(4-methylpiperazino)-2-propanole, 4-piperazinoaniline, 1-(3-chlorophenyl)piperazine diHCl (m-CPP), piperazin-2-one-HCl, 2-[4-(2-aminoethyl)-piperazin-1-yl] ethylamine, piperazine anhydrous, 2,4-diamino-6-phenyl-1,3,5-triazine, 3,5-diamino-1,2,4-triazole, melonamide, arginine-HCl, piperidine, 2,5-piperazinedione, piperazine, piperazin-2-one-HCl, 1-(2-pyrimidyl)piperazine dihydrochloride, or a pharmaceutically acceptable addition salt or hydrate thereof.

30. The use according to claim 29, wherein the compound is selected from 2-[4-(2-aminoethyl)piperazin-1-yl] ethylamine, 3-methylamino-1-(4-methylpiperazino)-2-propanole, and piperazine.

31. The use according to claim 1, wherein the compound is piperazine.

32. The use according to claim 1, wherein the compound is selected from 1,2-diaminoethane, 1,3-diaminopropane, 1,4-diaminobutane, 1,5-diaminopentane, 1,6-diaminohexane, 1,7-diaminoheptane, and 1,8-diaminooctane.

33. The use according to claim 1, wherein the compound is selected from 1,7-diaminoheptane, 1,2-diaminoethane, 1,4-diaminobutane, 1,6-diaminohexane, and 1,5-diaminopentane.

34. The use according to claim 1, wherein the compound is 1,6-diaminohexane.

35. The use according to any of the preceding claims, wherein the cell is from the kidney and/or the inner ear.

36. The use according to any of the preceding claims, wherein said compound in solution has at least 1, such as at least 2 positive charges, for example at least 20 positive charges.

37. The use according to any of the preceding claims, wherein said compound has a polybasic charge distribution.

38. The use according to claim 1, wherein the compound is a moiety of gentamicin, for the prophylaxis and/or treatment of induced cell toxicity, wherein said cell presents the receptor megalin and/or the receptor cubilin.

39. The use according to claim 38, wherein said compound is Garoseamine.

40. The use according to claim 38, wherein said compound is Purpurosamine.

41. The use according to claim 38, wherein said compound is 2-deoxystreptamine.

42. A compound having the general formula of

$$(A_q-X)_p \qquad \text{(VII)}$$

wherein
A is independently or in combination selected from formula (I) and/or formula (II) and/or formula (III) and/or formula (IV) and/or formula (V) and/or formula (VI), Garoseamine, Purpurosamine, and 2-deoxystreptamine, as defined in any one of claims 1-37, and wherein
X is a spacer,
q is an integer of 1-100,
p is an integer of 1-100.

43. The compound according to claim 42, wherein the spacer is a covalent bond.

44. The compound according to claim 42, wherein the spacer consists of from 2-12 atoms, such as C-atoms, for example from 4-10 atoms, such as C-atoms, preferably from 6-8 atoms, such as C-atoms.

45. Use of a compound as defined in claim 42 for the prophylaxis and/or treatment of induced cell toxicity.

46. Use of a compound as defined in claim 42, wherein the use is defined in any one of claims 1-37.

47. A combination medicament comprising a compound as defined in any of the claims 1-46 and a therapeutic agent for simultaneous, separate or sequential use in induced cell toxicity therapy.

48. The combination medicament according to claim 47, wherein said cell presents the receptor megalin and/or the receptor cubilin.

49. A pharmaceutical composition comprising a compound as defined in any of claims 42-44 and pharmaceutically acceptable carriers, excipients or diluents therefor.

50. A method for reducing cell toxicity of a therapeutic agent comprising at least one cell toxic compound, said method comprising reducing the number of cationic groups from said at least one cell toxic compound.

51. The method according to claim 50, wherein the cell toxicity is nephrotoxicity or ototoxicity.

52. The method according to claim 50 or 51, wherein at least one cationic group is an amino group.

53. The method according to any one of claims 50-52, wherein the compound comprises at least two cationic groups.

54. The method according to any one of claims 50-53, wherein the number of cationic groups is reduced by substituting at least one cationic group by another group.

55. The method according to claim 54, wherein the other group is selected from H, OH, and lower alkyl (C1-C4).

56. The method according to any one of claims 50-55, wherein the number of cationic groups is reduced by introducing an amide group into said compound.

57. The method according to any one of claims 50-56, wherein the therapeutic agent is selected from acebutolol, acetazolamide, acyclovir, adefovir, albumin, alclofenac, alendronate, alitretinoin, altretamine, amikacin, amiloride, aminoglutethimide, amiodarone, amoxicillin, amoxicillin/clavulanic acid, amphotericin b, amphotericin b cholesteryl sulfate complex, amphotericin b lipid complex, amphotericin b liposome, amtolmetin, aniracetam, antacids, antazoline, anthraquinone laxatives, aprotinin, arginine, arsenic trioxide, asparaginase, aspirin, atenolol, atovaquone, auranofin, aurothioglucose, azacitidine, azathioprine, azlo-

cillin, aztreonam, bacampicillin, bacitracin, bemetizide, benoxaprofen, betaine, bezafibrate, bismuth subcitrate, bleomycin, boric acid, brivudine, broxuridine, bumetanide, calcifediol, calcitriol, candesartan, candesartan/hydrochlorothiazide, canrenoate, capreomycin, captopril, carbenicillin, carboplatin, carmustine, carprofen, cefaclor, cefetamet, cefixime, cefmetazole, cefonicid, cefoperazone, cefoperazone/sulbactam, cefotaxime, cefotetan, cefoxitin, cefpirome, cefsulodin, ceftazidime, ceftezole, ceftibuten, ceftizoxime, ceftriaxone, cefuroxime, celecoxib, cephalexin, cephaloridine, cephalothin, cephapirin, cephradine, chlortetracycline, cidofovir, cilazapril, cimetidine, ciprofibrate, cisapride, cisplatin, clarithromycin, clodronate, clofibrate, cloxacillin, cocaine, codeine, colistin, corticotropin, cosyntropin, cotrimazine, cotrimoxazole, crisnatol, cyclacillin, cyclosporine, cysteamine, decitabine, delapril, delavirdine, demeclocycline, denileukin diftitox, desflurane, dextran, diatrizoate, diazoxide, dibekacin, diclofenac, diclofenac/misoprostol, dicloxacillin, dicumarol, didanosine, dihydroergotamine, dihydroergotamine/heparin, dihydrotachysterol, dirithromycin, dopamine, doxepin, doxorubicin hydrochloride liposome, doxycycline, edetate calcium disodium, edetate disodium, emetine, enflurane, enlimomab, epinephrine, epirubicin, ergocalciferol, ergotamine, erythromycin/sulfisoxazole, erythropoietins, ethanolamine oleate, ethyl chloride, etidronate, etodolac, etomidate, etretinate, everninomycin, fadrozole, fenbufen, fenofibrate, fenoprofen, fenoterol/ipratropium, flecainide, fleroxacin, floxacillin, flupirtine, flurbiprofen, formestane, foscarnet, fosinopril, fotemustine, framycetin, furosemide, gabexate, gadopentetate dimeglumine, gallium nitrate, gemcitabine, gemfibrozil, gentamicin, glycerin, gold sodium thiomalate, guanadrel, guanethidine, guar gum, halothane, hemiacidrin, hemin, hetastarch, homoharringtonine, hyaluronidase, hydrochlorothiazide, idarubicin, ifosfamide, imatinib, imipramine, indapamide, influenza vaccine, interferon alfa-2a, interferon alfa-2b, interferon beta, natural, interferon beta-1b, interferon gamma, interleukin-3, interleukin-4, interleukin-6, iobenguane I-131, iodixanol, iohexol, iopamidol, iopanoic acid, iopentol, iopromide, iotrolan, ioversol, ioxaglate, ioxilan, ioxithalamate, irinotecan, irofulven, isepamicin, isoflurane, isoniazid, isoxicam, kanamycin, ketamine, ketoconazole, ketoprofen, ketorolac, lenograstim, levofloxacin, lincomycin, liposomal nystatin, lisinopril, lithium, lobaplatin, lomustine, lonidamine, lornoxicam, losartan, loxapine, lymphocyte immune globulin, mannitol, mebendazole, mefenamic acid, meglumine antimoniate, melarsoprol, meropenem, mesna, metaraminol, methacycline, methicillin,

methimazole, methocarbamol, methotrexate, methoxamine, metrizamide, metronidazole, mezlocillin, milrinone, miltefosine, minocycline, minoxidil, mitoguazone, mitolactol, mitomycin, mitotane, molindone, morniflumate, morphine, moxalactam, muromonab-CD3, nabumetone, nafcillin, naproxen, nedaplatin, neomycin, netilmicin, niclosamide, nifedipine, niflumic acid, nifurtimox, nisoldipine, nitroprusside, norepinephrine, norfloxacin, ofloxacin, olsalazine, oxaliplatin, oxandrolone, oxaprozin, oxolinic acid, oxytetracycline, paclitaxel, pamidronate, paramethadione, paromomycin, pefloxacin, pemetrexed, pemirolast, penicillin G, pentamidine, pentostatin, peplomycin, perindopril, phenazopyridine, phenindione, phenobarbital, phenylbutazone, phenylpropanolamine, phenytoin, phosphates, piperacillin, pirarubicin, piretanide, piroxicam, plicamycin, poloxamer-188, polymyxin B, potassium perchlorate, praziquantel, proglumetacin, propylthiouracil, pyrimethamine/sulfadoxine, quinagolide, quinapril, quinine, rabbit antithymocyte globulin, raltitrexed, ranitidine, ranpirnase, recombinant human hemoglobin, rifampin, ritodrine, ritonavir, rofecoxib, rolitetracycline, rufloxacin, salsalate, sevoflurane, silver nitrate, silver sulfadiazine, simvastatin, sodium cellulose phosphate, sodium chloride, sodium fluoride, sodium stibogluconate, spironolactone, streptokinase, streptomycin, streptozocin, sulfamethoxazole, sulfasalazine, sulfinpyrazone, sulfisoxazole, sulindac, sulprostone, sultamicillin, suprofen, tacrolimus, tasonermin, teicoplanin, temafloxacin, teniposide, tenoxicam, tetracycline, thiopental, tiaprofenic acid, ticarcillin, ticrynafen, tiludronate, tiopronin, tobramycin, tocainide, tolazoline, tolmetin, torsemide, tramadol, triamterene, trimethadione, trimethaphan, trimethoprim, trimetrexate, trimipramine, troglitazone, tromethamine, typhoid vaccine, valsartan, vancomycin, zolimomab aritox, zomepirac, and zopiclone.

58. The method according to claim 57, wherein the therapeutic agent is selected from the group consisting of aminoglycosides, such as gentamicin, kanamycin, neomycin, paramycin, ribostamycin, lividomycin, amikacin, dibekacin, butakacin, tobramycin, streptomycin, dihydrostreptomycin, sisomicin, verdamicin, nefilmicin, and butikacin, cisplatin, amphotericin B, ifosfamide, polymyxin B, cyclophosphomide, methotrexate, aprotinin, ciclosporin, and valproate as well as therapeutic antibodies.

59. The method according to claim 57, wherein the therapeutic agent is an aminoglycoside.

60. A therapeutic agent comprising at least one compound being reduced in cell toxicity by a method as defined in any one of claims 50-59.

61. Use of a compound as defined in claim 60 for the preparation of a therapeutic agent for the treatment of a disease.